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14. ABSTRACT

Purpose To determine whether men diagnosed with prostate cancer make changes in dietary intake, physical activity, and use of dietary supplements, and the extent to which the changes differ by race (African American and Caucasian American), and to ascertain whether alterations in dietary intake and dietary supplement use upon a diagnosis of prostate cancer are associated with changes in oxidative DNA damage in lymphocytes and serum prostate specific antigen (PSA) levels.

Scope This project builds upon a Department of Defense-sponsored CaP Consortium, "Racial Differences in Prostate Cancer: Influences of Health Care and Host and Tumor Biology." For this longitudinal study, a subset of Consortium participants in North Carolina (125 African American, 125 Caucasian American) will be recruited and followed for a period of 2 years. Data will be collected at baseline by the Consortium and, in this study, at 12- and 24 months post-diagnosis using similar methodology.

Major findings: Institutional Review Board approval has been obtained from both the funding agency (i.e., the DoD) and from the University of North Carolina. Study staff have been hired and trained. Participant enrollment and data collection will begin in September 2006. An abstract describing the study design was presented at the 2006 Experimental Biology Annual Conference.

15. SUBJECT TERMS
prostate cancer; African Americans; diet; physical activity; supplement use; Caucasian Americans; prognosis; behavior

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Introduction

African Americans have the highest prostate cancer mortality rates among all racial/ethnic groups and recurrence rates for prostate cancer after definitive treatment have been shown to be significantly higher in African Americans (1-5). Research suggests that prostate cancer prognosis may be affected by lifestyle factors; however, there is little published data on patterns of health behaviors among men diagnosed with prostate cancer, and no available information on differences by race (2,6,7). The hypothesis of this study is that men diagnosed with prostate cancer modify lifestyle factors (dietary intake, physical activity, and dietary supplement use) differently by race, which alters prognosis. Specifically, African Americans diagnosed with prostate cancer make fewer healthy changes than Caucasian Americans, which might contribute to worse prognosis among African Americans. The objectives of the study are to determine whether men diagnosed with prostate cancer make changes in dietary intake, physical activity, and use of dietary supplements, and the extent to which the changes differ by race (African American and Caucasian American), and to ascertain whether alterations in dietary intake and dietary supplement use upon a diagnosis of prostate cancer are associated with changes in oxidative DNA damage in lymphocytes and serum prostate specific antigen (PSA) levels (a marker of prognosis) (8,9). To accomplish these aims, the study builds upon a Department of Defense-sponsored prostate cancer Consortium, "Racial Differences in Prostate Cancer: Influences of Health Care and Host and Tumor Biology." The Consortium is a population-based case-only study of newly diagnosed prostate cancer cases (age 40-80 years) in 42 North Carolina counties and 7 Louisiana Parishes. For this longitudinal study, we propose to recruit a subset of Consortium participants in North Carolina (125 African Americans, 125 Caucasian Americans) and follow them for a period of 2 years. Data will be collected at baseline by the Consortium and, in this study, at 12-, and 24-months later using the same methodology. Dietary intake, physical activity, and use of dietary supplements at each of the follow-up assessments will be collected using a computer-assisted instrument. Between 6 and 12-months after diagnosis, participants will complete 3-24 hour dietary recalls by telephone to assess current diet. Nutrient biomarkers (serum carotenoids and tocopherols), oxidative DNA damage in lymphocytes as measured by single-cell gel electrophoresis (alkaline Comet assay), and serum PSA levels will be assessed at 12- and 24-months. Oxidative DNA damage in lymphocytes and serum PSA levels will be used as objective markers of dietary effects and disease progression, respectively. All data will be collected by in-personal, in home interviews. This project will provide important information on changes in modifiable lifestyle factors among men diagnosed with prostate cancer, and the extent to which the changes differ by race. The determination of racial differences in health behaviors post-diagnosis may provide insights into disparities in prostate

cancer prognosis between African Americans and Caucasian Americans. Together, these data would provide information that could be used to develop appropriate interventions to lower the risk of fatal prostate cancer and reduce racial disparities in prostate cancer prognosis.

Body

The study has had a relatively slow start for a number of reasons. Dr. Jessie Satia, who wrote and submitted the original proposal, took an unpaid leave of absence from February 2004-March 2006. Her leave necessitated a change of Principal Investigator (PI). In November 2005, Dr. Steck-Scott who assumed the role of PI when Dr. Satia went on leave, left the University of North Carolina at Chapel Hill (UNC Chapel Hill) to pursue a faculty appointment at the University of South Carolina. There were also some delays in beginning data collection for the North Carolina-Louisiana Consortium. This is important because our study recruits participants who have already completed the main study (i.e., the Consortium) and agree to participate in this follow-up study. These events have resulted in the fact that data collection for the study has not yet begun. Nonetheless, since Dr. Satia returned to UNC in March 2006, she has been moving forward aggressively to begin data collection. Below, we present the current status of study activities described in the Statement of Work and updated timeline.

Task 1 Study design, set-up, and sampling of prospective participants

a) *Hire project staff – Dr.* Satia has recently hired all the staff necessary to work on the study. Study activities are being conducted by staff at the Center for Digestive Diseases and Biology (CGBID). The CGBID is a collaborative research center at UNC Chapel Hill that supports various research projects. Staff at the CGBID have extensive experience in the conduct of population-based epidemiologic studies, particularly those that include personal, in-home visits. The study manager, Ms. Shelby Dunivant, is a trained nurse and has extensive experience in project management. The rest of the study staff (database manager, programmer, biostatistician, enrollment specialists, and study nurses) are all highly experienced and valuable assets to the project.

b) *Design and develop tracking system for participant recruitment, acquisition of biological samples, and collection of self-reported data* – The tracking system has been designed and is currently being tested.

c) *Complete handbook detailing all protocols to be used* – The study manual has been prepared and is currently undergoing extensive review.

d) *Train 2 interviewers/phlebotomists (interviewers) in use of computer-assisted interviewing (training videos have been created and will be available from the Consortium (i.e., parent grant); and in the conduct of home interviews (by the nurse interviewers working on the Consortium)* – All study staff, including the nurse-interviewers are trained and ready to begin data collection in September.

Note: Pilot testing of interview instruments have been previously conducted by the parent study.

Task 2 Participant recruitment

a) Obtain Institutional Review Board approval for this ancillary study – IRB approval had been obtained from both the funding agency (i.e., the DoD) and from the UNC Chapel Hill Institutional Review Board. We have recently submitted a modification to the UNC IRB to reflect the change in PI and study staff.

b) *Obtain names of eligible participants from the Consortium* – This activity will begin in mid-August 2006, as soon as we receive a letter from the UNC IRB indicating that the modifications have been approved.

Note: All participants in this study have been identified by rapid case ascertainment from the North Carolina Registry, and baseline data collected by the parent study (i.e., the Consortium).

Task 3 Data collection I: 6-month follow-up

Note: In lieu of conducting a home visit at 6 months, we decided to collect information on current data using 3-24-hour dietary recalls that will be conducted by telephone. This decision was motivated by the fact that we felt that it would place additional burden on participants to do a detailed home interview 2-3 months after their baseline interviews in the main (Consortium) study, as the baseline interviews are being conducted on average 4-5 months after diagnosis, and we would be contacting potential participants approximately 5-6 months post-diagnosis. The 3 recalls will be spaced over a 6 month period. Upon completion of the last recall, our trained

nurses will schedule and complete the 12-month home visit. One year later, i.e., 24-months post diagnosis, the second home interview would be conducted.

Once participants in the Consortium complete the baseline interview, they would be sent a letter by the Consortium informing them about this follow-up study and requesting that they contact study staff if they do not wish to participate in the present study. If the participant does not indicate that he does not wish to be contacted within 2 weeks of the letter being mailed, our race-matched enrollment specialists will contact eligible participants by telephone to elicit participation. We will use a rolling recruitment method, recruiting all consecutive eligible men from the parent study, for a total sample size of 250 men. Those who agree to participate would be enrolled in the study. As noted above, they would then provide 3 unannounced 24-hour dietary recalls over the subsequent 6 months (approximately one every 2 months). Upon completion of the 3rd recall, participants should be at or close to 12-months post-diagnosis, and would then be scheduled for an in person at home interview that would be conducted by trained nurses - *This activity will begin in mid-August 2006, as soon as we receive a letter from the UNC IRB indicating that the modifications have been approved.*

Key Research Accomplishments

Study Activities

- In March 2006, the original PI, Dr. Jessie Satia, returned to UNC Chapel Hill from a leave of absence and has now been re-assigned as PI by the funding agency.
- We received UNC-CH Institutional Review Board (IRB) approval for the study questionnaires and communication materials in September 2005 and approval from the DoD HSRRB was also received in October 2005.
- In mid-July 2006, we submitted a modification to the UNC-CH IRB to reflect minor changes in the study personnel and materials since September 2005.
- All study staff for the project have been hired and trained.
- The study manual has been written and is being reviewed.
- The study database which will capture all aspects of the study ranging from participant recruitment, data collection, and tracking has been designed and is currently being tested.

Reportable Outcomes

An abstract describing the study design was submitted to the Experimental Biology Annual Meeting in April 2006 and was accepted as a poster presentation. A copy of the poster is enclosed.

Study Timeline

The study timeline is as follows:

Date	Activity
July 2006	IRB approval for modifications from UNC-CH IRB
August 2006 – September 2007	Recruitment and enrollment of all 250 participants, recruited approximately 5-6 months post-diagnosis
September 2006 – March 2008	Three 24-hour dietary recalls (telephone-administered)
March 2007 – March 2008	In-home visits 12 months post-diagnosis
March 2008 – March 2009	In-home visits 24 months post-diagnosis

Conclusions

In summary, although the start-up of the study has been slower than planned due to the unanticipated events noted above, we are moving aggressively to beginning data collection. The study design and set-up, including protocol, questionnaires and tracking system development, are on target. Participant recruitment and data collection are scheduled to begin in August 2006. In summary, the design of this follow-up study is as follows: after baseline data collection by the Consortium (approx. 4-5 months after prostate cancer diagnosis), information on current diet will be collected between 6 and 12 months post-diagnosis using 3-24 hour dietary recalls. At 12- and 24-months post diagnosis, additional self-reported interview data and biological samples (blood, toenails, and urine) will be collected using personal in home interviews. Final visits with all 250 participants are expected to be completed by March 2009. We appreciate the funding agency's support for this important project.

Relevance

This project will provide important information on changes in modifiable lifestyle factors (diet, physical activity, and dietary supplement use) among men diagnosed with prostate cancer, and the extent to which the changes differ by race. In particular, identification of dietary effects on prostate cancer prognosis would suggest the importance of lifestyle determinants in prostate cancer outcome. Additionally, the determination of racial differences in health behaviors post-diagnosis may provide insights into disparities in prostate cancer prognosis between African

Americans and Caucasian Americans. Together, these data would provide information that could be used to develop appropriate interventions to lower the risk of fatal prostate cancer and reduce racial disparities in prostate cancer.

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Appendix

A copy of the following poster is enclosed: Paxton A, Steck S, Kupper L, Arab L, Satia, J. Lifestyle Changes in African Americans and Whites Following a Diagnosis of Prostate Cancer: Rationale, Objectives, and Study Design. Experimental Biology Annual Meeting, April 2006, San Francisco, CA.

Lifestyle Changes in African Americans and Whites Following a Diagnosis of Prostate Cancer: Rationale, Objectives, and Study Design

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ABSTRACT #B143

Prostate Cancer (CaP) is the most common cancer in men and the second leading cause of cancer mortality. African Americans have the highest CaP incidence and mortality rates among all racial/ethnic groups. Research suggests that lifestyle changes may influence CaP outcomes post-diagnosis. The objectives of this study are to 1) assess changes in modifiable lifestyle factors (diet, dietary supplement use, and physical activity) post-diagnosis and determine whether changes differ by race, and 2) examine the extent to which lifestyle changes may influence CaP outcomes post-diagnosis as measured through changes in serum PSA. This report discusses the study rationale, objectives, and design. Newly diagnosed African American and White prostate cancer patients in North Carolina (n=250) will be followed for 2 years. Participants will complete three 24-hour dietary recalls between 6 and 12 months post-diagnosis. At 12- months and 24-months post-diagnosis, in-home interviews will be conducted that include anthropometric measurements; questionnaires related to dietary intake, physical activity, dietary supplements, and other lifestyle factors; and collection of biologic samples. Longitudinal data analysis methods will be used to examine changes in these lifestyle factors post-diagnosis in relation to serum PSA levels. Data collection is underway and the initial set of results is expected in 2007. Identification of modifiable lifestyle factors that affect CaP outcomes post-diagnosis and any differences by race may provide information that can be used to develop appropriate interventions to reduce racial disparities in CaP prognosis and lower the risk of fatal prostate cancer.

Program number 122.16

BACKGROUND

African Americans (AA) have higher incidence and mortality rates of prostate cancer (CaP) than Caucasian Americans (CA), and AA mortality rates in North Carolina are in the top three in the United States.[1] Dietary and lifestyle factors are associated with CaP risk and may be associated with prognosis.[2,3] However, data regarding lifestyle changes in response to a diagnosis of CaP are scarce. In addition, the racial disparity that exists in CaP is not yet well understood and deserves further attention. Thus, this study attempts to thoroughly examine possible racial differences in diet, physical activity and dietary supplement use following CaP diagnosis, and how these may be related to disease progression and prognosis.

HYPOTHESIS

Men diagnosed with CaP modify lifestyle factors (dietary intake and dietary supplement use) differently by race, which alters prognosis. Specifically, AA men will make fewer healthy changes than CA, which might contribute to worse prognosis among AA.

STUDY AIMS

Primary Aims

1) Investigate changes in dietary intake from self-report (total energy; carotenoids; vitamin E; calcium/vitamin D; fats/fatty acids; and isoflavones) and serum biomarkers (carotenoids and tocopherols) between baseline and the 12- and 24-month time points, and whether changes differ by race.

2) Examine changes in frequency, types, and/or doses of vitamin, mineral and herbal supplements between baseline and 12-, and 24-months, and whether changes differ by race.

Secondary Aims

3) Examine whether changes in dietary intake and/or physical activity are associated with lymphocyte oxidative DNA damage, a biomarker of diet and possibly, disease progression.

4) Examine whether changes in dietary intake and/or physical activity are associated with CaP prognosis using serum PSA as intermediate endpoint of disease progression.

METHODS

OVERVIEW

Participants will complete three 24 hour recalls over the telephone, and two in-home interviews, which include lifestyle factors questionnaires, anthropometric measurements, and blood, toenail, and urine sample collection.

RECRUITMENT

•This study is a follow-up study of the CaP patients enrolled in a Dept. of Defense (DoD)-sponsored CaP Consortium. Eligible subjects will be selected from North Carolina patients in the CaP Consortium

•Participants will be recruited from a 18-county area of North Carolina. Contact with each patient will be made by mail with an introductory letter describing the study and inviting participation.

•250 participants (125 AA and 125 CA)

INCLUSION CRITERIA

- Newly diagnosed CaP cases age 40-80 years old.
- Must be free of cognitive impairments and language or hearing problems.
- English written and oral fluency
- Live in a private residence
- Able to provide informed consent

DATA COLLECTION

24-Hour Dietary Recalls

•Participants are contacted unannounced by phone on at least three different days, between 6 and 12 months post-diagnosis, provide verbal informed consent, and are asked to report all foods and beverages consumed *during the previous day* to estimate current dietary intake.

In-Home Interviews

•At 12 and 24 months post-diagnosis, trained nurse interviewers visit participants at home to obtain informed consent, conduct interviews and collect biological samples and anthropometric measurements.

Questionnaires used during In-Home Interviews

•National Cancer Institute Diet History Questionnaire, modified to include foods consumed specific to North Carolina.

•This questionnaire is administered once in the parent PCaP study to determine usual diet prior to diagnosis.

•Data from the follow-up study will be compared to the baseline data to assess dietary change following diagnosis.

•Physical Activity Questionnaire

•Lifestyle Change Questionnaire, which will capture changes in diet, supplement use, and physical activity after CaP diagnosis.

Biological Markers

Blood

- 40cc of semi-fasting blood will be drawn in-home by a trained nurse interviewer.
- Tocopherol and carotenoid concentrations will be measured in serum by High Performance Liquid Chromatography
- Oxidative DNA damage in lymphocytes will be measured in lymphocytes using the modified alkaline COMET assay.

Urine

- 100cc of a "spot" urine sample will be collected during the in-home visit and stored for future analyses.

Toenail Clippings

- Participants will collect clippings of their toenails, from each toe on one foot, prior to the in-home interview and stored for future analyses.

Medical Record Abstraction

- PSA levels will be obtained by medical record abstraction

ANALYSIS

- Except for the Lifestyle Change Questionnaire, all data collected in this study are also being collected in the parent study to obtain baseline (pre-diagnosis) information.
- Changes in the exposures of interest will be assessed by comparing baseline and follow-up information using longitudinal data analysis methods with control for confounding factors.

APPLICATIONS

•Identification of racial differences in health behaviors post-diagnosis may provide insights into disparities in prostate cancer prognosis between AA and CA

•A finding of racial differences in diet, use of dietary supplements and/or physical activity among men diagnosed with CaP would provide rationale for randomized trials targeting the most important nutrients or lifestyle factors in the appropriate group.

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